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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,622	01/14/2005	Takeshi Hagio	59150-8030	2017

22918 7590 07/09/2008

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EXAMINER	
FERNANDEZ, SUSAN EMILY	
ART UNIT	**PAPER NUMBER**
1651	

NOTIFICATION DATE	DELIVERY MODE
07/09/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Office Action Summary	Application No.	Applicant(s)	
	10/521,622	HAGIO ET AL.	
	Examiner	Art Unit	
	SUSAN E. FERNANDEZ	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,6,8-27,29-48 and 71* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,6,8-27,29-48 and 71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment and declaration filed April 7, 2008, has been received and entered.

Claims 2, 3, 5, 7, 28, and 49-70 are cancelled. Claims 1, 4, 6, 8-27, 29-48, and 71 are pending and examined on the merits to the extent they read on the elected subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4, 6, 8-27, 29-48, and 71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 27 are indefinite since it is unclear where in the recited steps the transfer of nucleic acid occurs. It is unclear in claim 27 how the nucleic acid is introduced. Thus, claims 1, 4, 6, 8-27, 29-48, and 71 are rejected under 35 U.S.C. 112, second paragraph.

Claims 8, 10, and 15 are indefinite since they depend from a canceled claim, claim 7. Claims 8-26 are thus rejected under 35 U.S.C. 112, second paragraph. For examination purposes, claims 8-26 each will be read as the method according to claim 1.

Claim 27 is indefinite since the recitation "the cell" in step a) lacks antecedent basis as the preamble of the claim recites "the cells of a plant." Thus, claims 27, 29-48, and 71 are rejected under 35 U.S.C. 112, second paragraph.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4, 6, 8-27, 29-48, and 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dodgson et al. (WO 00/63407, listed on IDS) in view of Gutierrez-Armenta et al. (US 2002/0046416) and Dev et al. (US 5,859,327).

Dodgson et al. discloses a method of introducing a substance into a cell, which can be the transfection of a cell (abstract). One embodiment of the invention is the introduction of DNA into living cells "…by rupturing or forming a discontinuity in the cell wall by the process of electroporation" (page 3, lines 20-21). Prior to the transfection of cells, the cells are sorted, and this can be achieved by directed pressure pulses (page 9, lines 1-5). Figure 4e shows an embodiment of the invention wherein pressure is applied to cells to be transfected. The cell is

localized against the orifice of a channel which contains the transfection material by a force created by a pressure drop (page 14, line 20 through page 15, line 2). Furthermore, electrodes may be included to electroporate the cell membrane around the orifice of the channel (page 15, lines 9-10). Clearly Dodgson et al. teaches a method for transferring a nucleic acid into a cell, wherein first a pressure different from an atmospheric pressure is applied, followed by electroporation. Moreover, Dodgson et al. teaches that a microprocessor is used to modify one or more system parameters, including the pumping pressure (page 17, lines 17-18). Given that there is such a control on the pumping pressure, depressurization is indeed taught by the reference.

Dodgson et al. differs from the claimed invention in that it does not expressly disclose that the depressurization step is performed under a pressure reduced by about 0.096 MPa from the atmospheric pressure, as required by claims 1 and 27. Nevertheless, the selection of a specific suitable pressure, including that claimed, would have been an obvious matter of optimization on the part of the artisan of ordinary skill, particularly since Dodgson et al. teaches varying the pressure applied (page 17, lines 2-3 and 17-18).

Furthermore, Dodgson et al. differs from the claimed invention in that it does not expressly disclose that the cell treated is a plant cell of the types recited in instant claims 10-26 wherein the steps can be performed on a seed, and that the treated plant cell differentiates/grows/multiplies and/or yields a plant which may not contain a somaclonal variation. Moreover, there is no disclosure in Dodgson et al. that the voltage pulse applied to the cell is of 10 V/cm to 200 V/cm, which is applied to the cell and the nucleic acid in at least two directions.

Gutierrez-Armenta et al. discloses that cell growth may be controlled by administering DNA to a cell, and that the DNA may be administered by electroporation of plant seed cells with DNA (page 2, paragraph [0015]).

Dev et al. teaches "a method for producing a genetically modified plant by introducing a polynucleotide to an intact plant or plant cell(s) via electroporation, in the absence of cell wall-degrading enzymes" (abstract). The "plant cell" may be an intact cell of a seed (column 4, lines 15-17), wherein the recitation "intact" signifies that the cell wall is undamaged or untreated (column 4, lines 20-22). The method can be applied to monocotyledonous plants such as corn, wheat, rice, and dicotyledonous plants such as tomato, rapeseed, soybeans, and cabbage (column 6, lines 15-25). Moreover, Dev et al. indicates that "one of skill in the art could determine the appropriate parameters for the leaf type used" (column 8, lines 62-63). For instance, a voltage of 40-50 V/cm for electroporation, which is within the range recited in instant claim 6, is deemed suitable for "soft and thin" leaves (column 8, lines 63-65).

At the time the invention was made, it would have been obvious to have practiced the invention on plant cells, which can be contained in seeds, to produce plants which may not contain a somaclonal variation. One of ordinary skill in the art would have been motivated to do this since electroporation has been found to be suitable for administering DNA to plant seed cells, and therefore, there would have been a reasonable expectation of success in transferring nucleic acid into plant cells to produce a plant by the methods of Dodgson et al. which uses electroporation for nucleic acid transfer into cells. Additionally, there would have been a reasonable expectation of success in transferring nucleic acids into cells of plants of the types recited in the instant claims to yield the predictable result of producing these plants.

Also, the selection of a specific suitable voltage pulse and voltage pulse application directions, including that claimed, would have been an obvious matter of optimization on the part of the artisan of ordinary skill, particularly since Dodgson et al. teaches that the electrodes "…may advantageously be shaped in order to concentrate field and/or localize poration" (page 15, lines 22-23). Also, Dev et al. demonstrates that the skilled artisan would determine the appropriate parameters for the leaf type used, and Dev et al. teaches that electroporation applied at a voltage of 40-50 V/cm, which is within the range recited in instant claim 6, is deemed suitable the introduction of a polynucleotide to "soft and thin" leaves. Moreover, Dev et al. provides further support for administering DNA into cells of plants of the types recited in the instant claims by electroporation.

Thus, a holding of obviousness is clearly required.

Claims 1, 4, 6, 8-27, 29-48, and 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schmukler (US 5,173,158) in view of Gutierrez-Armenta et al. and Dev et al.

Schmukler teaches a method of electroporation wherein cells are trapped into pores in a film with diameters smaller than the diameters of the cells, and an electric field is applied to cause electroporation of the trapped cells (column 1, line 60 through column 2, line 3). The cells can be trapped into the pores by pressure such as hydrostatic pressure head from a regulated pressure source or a vacuum source (column 3, lines 20-26). Clearly the pressure applied to the cells must be different from atmospheric pressure. Thereafter, a low voltage pulse is applied which causes electroporation of the cells (column 3, lines 27-34). It is noted that "when the pressure gradient across the film is negative, or decreases from a positive value, the trapped first

type of cells will pull in material, such as genetic material (DNA)…" from a portion of the apparatus used to perform the Schmukler invention (column 3, lines 44-47). Thus, the cells are exposed to depressurization.

Schmukler differs from the claimed invention in that it does not expressly disclose that the depressurization step is performed under a pressure reduced by about 0.096 MPa from the atmospheric pressure, as required by claims 1 and 27. Nevertheless, the selection of a specific suitable pressure, including that claimed, would have been an obvious matter of optimization on the part of the artisan of ordinary skill, particularly since Schmukler teaches regulation of pressure applied (column 3, lines 20-26).

Furthermore, Schmukler differs from the claimed invention in that it does not expressly disclose that the cell treated is a plant cell of the types recited in instant claims 10-26 wherein the steps can be performed on a seed, and that the treated plant cell differentiates/grows/multiplies and/or yields a plant which may not contain a somaclonal variation. Moreover, there is no disclosure in Schmukler that the voltage pulse applied to the cell is of 10 V/cm to 200 V/cm, which is applied to the cell and the nucleic acid in at least two directions.

Gutierrez-Armenta et al. discloses that cell growth may be controlled by administering DNA to a cell, and that the DNA may be administered by electroporation of plant seed cells with DNA (page 2, paragraph [0015]).

Dev et al. teaches "a method for producing a genetically modified plant by introducing a polynucleotide to an intact plant or plant cell(s) via electroporation, in the absence of cell wall-degrading enzymes" (abstract). The "plant cell" may be an intact cell of a seed (column 4, lines 15-17), wherein the recitation "intact" signifies that the cell wall is undamaged or untreated

(column 4, lines 20-22). The method can be applied to monocotyledonous plants such as corn, wheat, rice, and dicotyledonous plants such as tomato, rapeseed, soybeans, and cabbage (column 6, lines 15-25). Moreover, Dev et al. indicates that "one of skill in the art could determine the appropriate parameters for the leaf type used" (column 8, lines 62-63). For instance, a voltage of 40-50 V/cm for electroporation, which is within the range recited in instant claim 6, is deemed suitable for "soft and thin" leaves (column 8, lines 63-65).

At the time the invention was made, it would have been obvious to have practiced the invention on plant cells, which can be contained in seeds, to produce plants which may not contain a somaclonal variation. One of ordinary skill in the art would have been motivated to do this since electroporation has been found to be suitable for administering DNA to plant seed cells, and therefore, there would have been a reasonable expectation of success in transferring nucleic acid into plant cells to produce a plant by the methods of Schmukler which uses electroporation for nucleic acid transfer into cells. Additionally, there would have been a reasonable expectation of success in transferring nucleic acids into cells of plants of the types recited in the instant claims to yield the predictable result of producing these plants.

Also, the selection of a specific suitable voltage pulse and voltage pulse application directions, including that claimed, would have been an obvious matter of optimization on the part of the artisan of ordinary skill, particularly since Schmukler teaches regulation of pressure applied (column 3, lines 20-26). Also, Dev et al. demonstrates that the skilled artisan would determine the appropriate parameters for the leaf type used, and Dev et al. teaches that electroporation applied at a voltage of 40-50 V/cm, which is within the range recited in instant claim 6, is deemed suitable the introduction of a polynucleotide to "soft and thin" leaves.

Moreover, Dev et al. also provides further support for administering DNA into cells of plants of the types recited in the instant claims by electroporation.

A holding of obviousness is clearly required.

Claims 1, 4, 6, 8-27, 29-48, and 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rickwood (WO 01/05994, listed on IDS) in view of Dev et al. (US 5,859,327).

Rickwood discloses a method of introducing a substance into a cell wherein bubbles containing gas are generated in a liquid medium comprising the cell, and the bubble interacts with the cell to form a hole in the surface of the cell (page 2, last paragraph through page 3, first paragraph). The substance that can be introduced into a cell can be a nucleic acid (page 8, last paragraph). Transfection of the cells occurs at pressure below and above atmospheric pressure, such as a pressure of from $1x10^4$ Pa to atmospheric pressure (page 6, last paragraph). Thus, the cell is subjected to depressurization. Finally, the Rickwood method can be performed on plant cells (page 9, first paragraph).

Rickwood differs from the claimed invention in that it does not expressly disclose that the cell and nucleic acid are placed under conditions to induce electroporation, such as the application of a voltage pulse of 10 V/cm to 200 V/cm in at least two directions. Moreover, Rickwood does not expressly disclose that the plant cells treated are of the types recited in instant claims 10-26 wherein the steps can be performed on a seed, and that the treated plant cell differentiates/grows/multiplies and/or yields a plant which may not contain a somaclonal variation.

Dev et al. teaches "a method for producing a genetically modified plant by introducing a polynucleotide to an intact plant or plant cell(s) via electroporation, in the absence of cell wall-degrading enzymes" (abstract). The "plant cell" may be an intact cell of a seed (column 4, lines 15-17), wherein the recitation "intact" signifies that the cell wall is undamaged or untreated (column 4, lines 20-22). The method can be applied to monocotyledonous plants such as corn, wheat, rice, and dicotyledonous plants such as tomato, rapeseed, soybeans, and cabbage (column 6, lines 15-25). Moreover, Dev et al. indicates that "one of skill in the art could determine the appropriate parameters for the leaf type used" (column 8, lines 62-63). For instance, a voltage of 40-50 V/cm for electroporation, which is within the range recited in instant claim 6, is deemed suitable for "soft and thin" leaves (column 8, lines 63-65).

At the time the invention was made it would have been obvious to have applied electroporation in addition to the steps recited in Rickwood. One of ordinary skill in the art would have been motivated to do this since electroporation assists in the introduction of genetic material to plant cells, as demonstrated in Dev et al. Moreover, it would have been obvious to one of ordinary skill in the art to apply electroporation as taught in Dev et al., to improve the genetic transfection method of Rickwood for the predictable result of introducing a substance into plant cells. The selection of a specific suitable voltage pulse and voltage pulse application directions, including that claimed, would have been an obvious matter of optimization on the part of the artisan of ordinary skill, particularly since Dev et al. demonstrates that the skilled artisan would determine the appropriate parameters for the leaf type used, and Dev et al. noted teaches that electroporation applied at a voltage of 40-50 V/cm, which is within the range recited in instant claim 6, is deemed suitable the introduction of a polynucleotide to "soft and thin" leaves.

Additionally, there would have been a reasonable expectation of success in transferring nucleic acids into cells of plants of the types recited in the instant claims and the Dev reference to yield the predictable result of producing these plants.

Though Rickwood does not expressly disclose that the depressurization step is performed under a pressure reduced by about 0.096 MPa from the atmospheric pressure, the selection of a specific suitable pressure, including that claimed, would have been an obvious matter of optimization on the part of the artisan of ordinary skill. Moreover, in reference to pressure conditions for transfection, Rickwood indicates that "Transfection can be carried out under widely varying conditions" (page 6, last paragraph).

Thus, a holding of obviousness is clearly required.

Response to Arguments

Applicant's arguments and the declaration filed April 7, 2008, have been fully considered but they are not persuasive. With respect to Dodgson, applicant argues that Dodgson neither shows nor suggests enhanced transfection efficiency by depressurizing cells in order to produce a large amount of nucleic acid-transferred matter. However it is noted that the features upon which applicant relies (i.e., enhanced transfection efficiency) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

With respect to Schmukler, the applicant asserts that there is no suggestion that the disclosed method is effective to introduce nucleotides into cells having a cell wall. However, it

is respectfully noted that the instant claims do not recite this limitation. Furthermore, applicant asserts that the Schmukler method is not applicable to plant seeds since they are too large to be retained on film which is used for practicing the Schmukler method. However, the applicant has not provided evidence to support this assertion. As pointed out in MPEP 2145, Section I, "The arguments of counsel cannot take the place of evidence in the record." Further still, MPEP 716.01(c), Section I, indicates that "Objective evidence which must be factually supported by an appropriate affidavit or declaration to be of probative value includes evidence of unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant."

The applicant also indicates that the Rickwood reference does not show or suggest that it is effective in introducing nucleotides into cells having a cell wall. However, as pointed out above, the claims under examination do not recite this limitation. Nevertheless, this limitation is indeed taught by Rickwood (page 9, first paragraph, last sentence).

The applicant asserts that Gutierrez-Armenta only discloses the possibility of electroporation of plant cells with DNA. However, the prior art is presumed to be operable and the burden is on the applicant to provide facts rebutting the presumption of operability. It is noted that Dev et al., the newly cited reference, provides further support to demonstrate that electroporation is suitable for use with plant cells. Moreover, the instant claims do not have any limitations regarding the presence of cell walls.

In regards to the declaration filed April 7, 2008, it is respectfully noted that the use of a pressure reduced by about 0.096 MPa from the atmospheric pressure is indeed rendered obvious

by the references used, thus similar results would have been obtained by the disclosures of Dodgson and Gutierrez-Armenta.

Though Schmukler and Rickwood do not expressly disclose depressurization of plant cells to a pressure 0.096 MPa below atmospheric pressure, the selection of a specific suitable pressure, including that claimed, would have been an obvious matter of optimization on the part of the artisan of ordinary skill, particularly since Schmukler teaches regulation of pressure applied (column 3, lines 20-26). Further still, the claims under examination do not require that pressure is being used to enhance electroporation of the cells, thus the prior art is not required to teach this limitation.

Given that the Rickwood invention can be performed on cells with cell walls such as plant cells (page 9, first paragraph), the cell wall of a plant can indeed be penetrated by the formation of holes in the surface of the cell. Moreover, the claims under examination do not recite any specifics as to the penetration of the cell wall of a plant seed. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSAN E. FERNANDEZ whose telephone number is (571)272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford/
Primary Examiner, Art Unit 1651

Susan E. Fernandez
Examiner
Art Unit 1651

sef